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# **The 1-min sit-to-stand test – a simple functional capacity test in cystic fibrosis?**

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## **Online supplementary material**

### **Methods**

#### *Participants*

Patients with CF who participated in a three-week pulmonary rehabilitation in Gran Canaria in November/December 2014 were included. All participants were required to send in a sputum sample and a precise personal history prior to pulmonary rehabilitation. Patients with *Burkholderia cepacia* complex and methicillin-resistant *Staphylococcus aureus* (MRSA) without *Pseudomonas* infection were excluded. The rehabilitation program took part in a large hotel where each patient had his/her own room. The program included a daily 30-min outdoor supervised group exercise session including gymnastics and strengthening exercises in the morning and a second supervised exercise session (e.g. tennis, volleyball) in the afternoon lasting 60-90 min. Furthermore, participants received daily individual chest physiotherapy in a segregated fashion (mainly airway clearance supervised by an experienced physiotherapist) for 45 min. Utmost precautions were taken to prevent cross-infection, including proper disinfection of rooms and materials, hand disinfection, no direct body contact, and diagnostic and therapeutic sequence according to resistance of pulmonary pathogens [1]. All participants provided written informed consent. Ethical approval was obtained from the cantonal ethical committee of Zurich, Switzerland.

### *Pulmonary function testing*

Spirometry was performed at the beginning and the end of the pulmonary rehabilitation in sitting position using a commercially available system (METAMAX<sup>®</sup> 3B, Cortex Biophysik GmbH, Leipzig Germany) according to ATS/ERS standards [2]. Percent predicted values were calculated for forced expiratory volume in 1s (FEV<sub>1</sub>) and forced vital capacity (FVC) based on equations recently published by Quanjer et al [3].

### *1-Minute sit-to-stand test*

The 1-min STS test was performed on a conventional chair without armrest (height of the seat: 46-48 cm to reach a knee angle of a visually determined 90° angle). Each STS test consisted of a 1-min rest phase with the participant sitting quietly on a chair followed by the 1-min STS exercise and a 3-min recovery phase with the participant sitting on the chair. During the active phase, the participants were instructed to stand-up and sit-down as often as possible at a self-chosen speed over one minute and they were allowed to stop anytime during the test. When standing up, the legs had to be fully straight and when sitting down, the buttock had to have clear contact with the chair. Heart rate (Polar<sup>®</sup> chest belt) and SaO<sub>2</sub> (Nonin<sup>®</sup> Xpod<sup>®</sup> PureSAT<sup>®</sup>, (METAMAX<sup>®</sup> 3B, Cortex Biophysik GmbH, Leipzig Germany) were continuously monitored during the test. At the end of the 1-min STS exercise, ratings of perceived exertion and dyspnea were evaluated by means of a 0-10 Borg scale. An illustration of a STS test with additional measurement of expired gases in a 27 year-old male patient with severe CF lung disease (FEV<sub>1</sub> 38% predicted) is presented in Figure S1.

All participants performed five STS tests during the pulmonary rehabilitation program. The first test (STS<sub>0</sub>) on day 2 of the program was considered a practice trial to familiarise the participants with the testing procedures. The second STS test (STS<sub>1</sub>) on day 3 was used as baseline test. The last three STS tests (STS<sub>2a-2c</sub>) were performed at the end of the rehabilitation program on day 17 and day 19 for the purpose of testing test-retest reliability

[4]. For logistical reasons (CPET had to be performed on all subjects during the same days), seven participants performed two STS tests ( $STS_{2a,b}$ ) at day 17 and one test on day 19 ( $STS_{2c}$ ) of the pulmonary rehabilitation program and seven participants performed one STS test ( $STS_{2a}$ ) at day 17 and two STS tests ( $STS_{2b,c}$ ) on day 19. A 15-minute rest was provided in-between the two repetitive STS tests. The sequence of testing was based on “malignancy” of pulmonary pathogens, but participants abstained from heavy exercise on the testing day and the physiotherapy session was always performed afterwards.

#### *Cardiopulmonary exercise testing*

CPET was performed after the STS test at the beginning (day 2 or day 3) and at the end (day 17 or 19) of the pulmonary rehabilitation program on a cycle ergometer (Lode Corival 906900, Lode BV, Groningen, Netherlands) using the Godfrey protocol [5]. The metabolic cart (METAMAX<sup>®</sup> 3B, Cortex Biophysik GmbH, Leipzig Germany) was calibrated with gases of known standard concentrations at each testing day. Heart rate was measured with a chest belt (Polar<sup>®</sup>) and oxygen saturation ( $SaO_2$ ) was measured at the earlobe using a Nonin<sup>®</sup> Xpod<sup>®</sup> PureSAT<sup>®</sup> sensor both connected with the metabolic cart. Ratings of perceived exertion and dyspnea were evaluated at peak exercise by means of a 0-10 Borg scale [6]. Three of the following criteria had to be fulfilled to ensure the test was maximal: 1) plateau in  $VO_2$  despite an increase in workrate; 2) peak heart rate over 85% of predicted [7], respiratory exchange ratio (RER) > 1.05, 4) peak ventilation exceeded predicted maximum voluntary ventilation (calculated as  $FEV_1 \times 35$ ) and 5) subjective impression of the supervisor. Data for peak $VO_2$  and maximum power are presented as % predicted values [8].

#### *Health related quality of life*

Health-related quality of life (HRQoL) was assessed with the revised adolescent and adult version of the German Cystic Fibrosis Questionnaire (CFQ-R) at the beginning and end of the

pulmonary rehabilitation [9]. The CFQ-R is a self-administered and disease-specific health-related questionnaire with five generic scales (physical functioning, vitality, emotional state, social limitations, role limitations), four disease-specific scales (feelings of embarrassment about symptoms, eating disturbance, body image, treatment burden), one scale on the subjective general health perception, and three scales assessing respiratory symptoms, digestive symptoms and weight problems. For each scale, the score is given on a 0- to 100-point scale with higher scores denoting higher HRQoL. We limited our analysis to the scales physical functioning and respiratory symptoms, as they were considered responsive to a rehabilitation program. The respiratory symptom scale served as anchor to estimate the minimal important difference (MID) for the STS [10].

#### *The Feeling Thermometer*

The Feeling Thermometer is a modified visual analogue scale in form of a thermometer. The instrument has marked intervals from 0 (worst health state = dead) to 100 (perfect health) and has been used in respiratory research [11, 12].

#### **Statistical analysis**

Data are presented as median (interquartile range, IQR) or means and standard deviations. All statistical analyses were performed with the statistical software package SPSS version 22 (IBM Corp. Armonk, NY, USA). The significance level was set at  $P < 0.05$ .

#### *Learning effect*

To document a possible learning effect for STS test performance, we analysed differences in the median number of repetitions between the first two STS tests (STS<sub>0</sub> and STS<sub>1</sub>) using a non-parametric Wilcoxon signed-rank test.

### *Test-retest reliability*

The median number of repetitions between the three reliability STS tests (STS<sub>2a-2c</sub>) were analysed with the non-parametric Friedman Test. Precision of STS test repetitions and measured variables during the STS tests (heart rate, SaO<sub>2</sub>, exertion and dyspnea) were quantified by the intra-individual standard deviations (SD<sub>within subjects</sub>) calculated by the root-mean-square (RMS) method and the coefficient of variation (CV/SD<sub>within subjects</sub> /overall mean) [4]. For three-point measurements at least 14 participants (51 exams) were needed to obtain valid precision errors using the RMS method [4]. Agreement between the three reliability STS tests (STS<sub>2a-2c</sub>) was investigated by the method of Bland and Altman [13]. We calculated intraclass correlation coefficients (ICC's) for the STS tests to estimate reliability using a two-way random model.

### *Construct validity*

To determine construct validity, correlations between STS test repetitions (mean number of STS test repetitions from STS<sub>2a-2c</sub>) and peakVO<sub>2</sub>, pulmonary function, patient-reported health status and HRQoL (post rehabilitation values) were analysed with linear regression analysis.

### *Minimal important difference*

To estimate the MID for the STS test, we used anchor-based and distributional methods [14]. The previously estimated MID of the respiratory symptoms scale (change of 4 units in stable CF patients) from the CFQ-R questionnaire was used as anchor to estimate the MID of the STS test [10]. Correlations between changes in STS test performance and the respiratory symptom scale were estimated with linear regression analysis. We further used a distributional method (0.5 SD) to estimate the MID, where the SD of the baseline test (STS<sub>1</sub>) is multiplied by 0.5.

## *Responsiveness to pulmonary rehabilitation*

We calculated Cohen's effect size to evaluate changes in outcome variables after pulmonary rehabilitation.

## **Results**

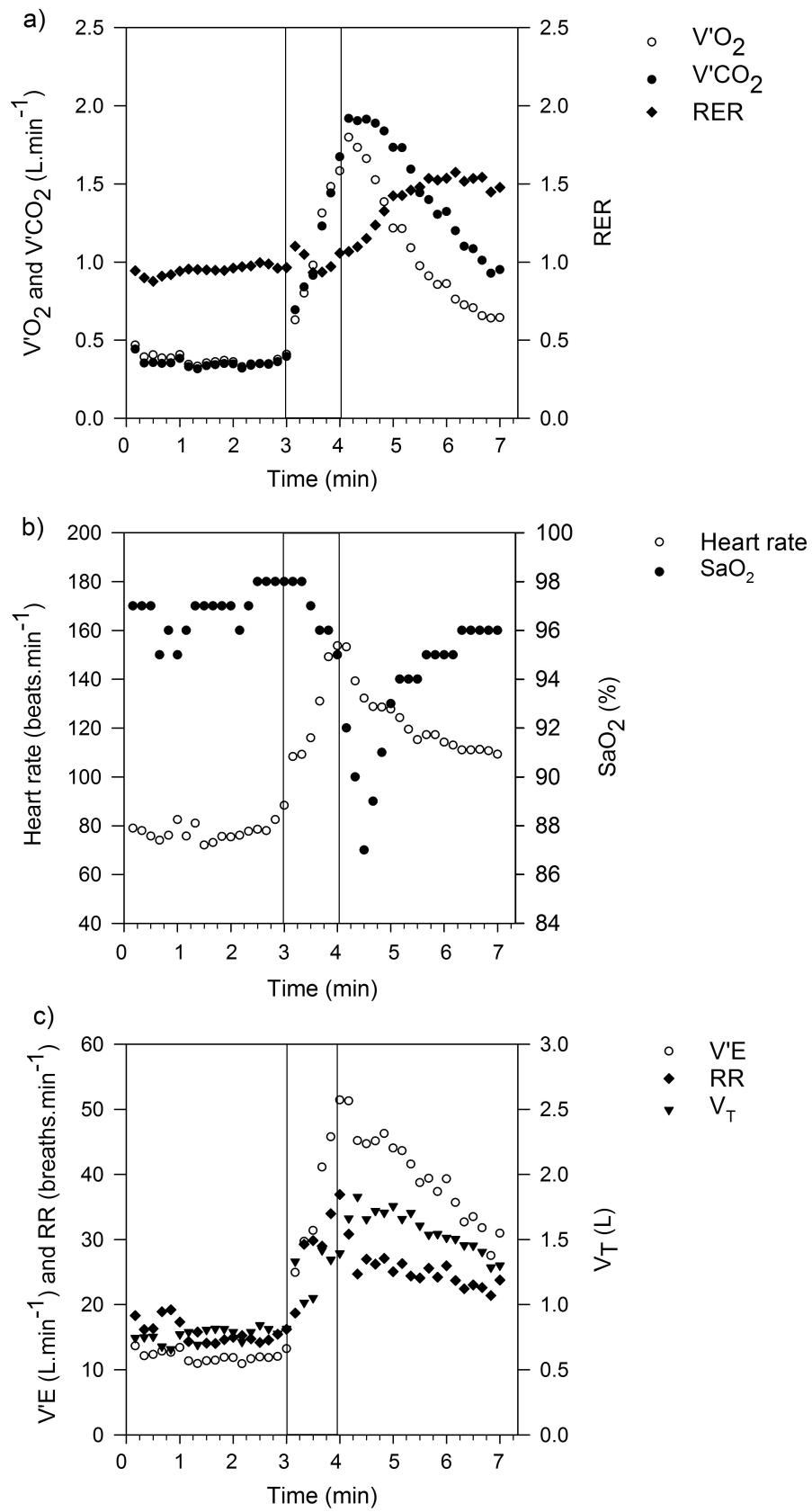
### *Study population*

Sixteen participants with CF took part in the pulmonary rehabilitation and performed all tests. Of those, data from two participants were excluded from the final analysis due to an unexpected death of a family member that reduced rehabilitation time and affected HRQoL assessments.

### *Sit-to stand test*

Figure S1 shows an illustration of a STS test with online gas analysis.

**Figure S1.** Illustration of a sit-to-stand (STS) test with measurement of expired gases in a 27-year old patient with severe cystic fibrosis lung disease. Data were recorded breath-by-breath but shown as 10 s averages. The total test duration was 7 minutes: 3 min rest, 1-min STS test and 3 min recovery. The black box between 3 and 4 min indicates the 1-min STS exercise period.  $\dot{V}O_2$ , oxygen consumption;  $\dot{V}CO_2$ , carbon dioxide production; RER, respiratory exchange ratio;  $SaO_2$ , oxygen saturation; RR, respiratory rate;  $V_T$ , tidal volume;  $\dot{V}E$ , minute ventilation. Borg dyspnoea score was 9 after completion of the 1-minute exercise. Compared to a maximal cardiopulmonary exercise test using the Godfrey cycle protocol  $\dot{V}O_2$  at the end of the 1 min STS test reached 56%,  $\dot{V}CO_2$  46%, heart rate 84%;  $\dot{V}E$  61%;  $V_T$  61%; RR 100% and minimum  $SaO_2$  96%.





### Test-retest reliability

Table S1: Reliability characteristics of sit-to-stand test parameters. Data are from three STS tests at the end of a rehabilitation program.

Parameter	Median (IQR)	Mean $\pm$ SD	SD <sub>within</sub> subjects	CV, %	ICC
STS <sub>2a</sub>	65.0 (55.8, 67.0)	62.4 $\pm$ 8.2	-	-	-
STS <sub>2b</sub>	67.0 (57.0, 70.5)	64.7 $\pm$ 8.4	-	-	-
STS <sub>2c</sub>	66.5 (59.8, 72.5)	66.1 $\pm$ 9.2	-	-	-
Mean number of repetitions from STS <sub>2a-c</sub> (N)	67.3 (57.5, 70.3)	64.5 $\pm$ 8.5	2.87	3.84	0.984
Peak heart rate (beats.min <sup>-1</sup> )*	151.2 (145.3, 159.3)	151.2 $\pm$ 10.8	5.84	3.86	0.913
Minimum SaO <sub>2</sub> (%)*	93.0 (85.7, 94.4)	90.9 $\pm$ 4.7	1.39	1.53	0.978
Dyspnea (0-10 scale) *	2.8 (2.2, 7.1)	4.3 $\pm$ 2.8	1.28	60.09	0.933
Borg exertion (0-10 scale)*	6.3 (3.7, 8.2)	6.1 $\pm$ 2.4	0.97	16.37	0.950

Data are based on three sit-to-stand tests. CV, coefficient of variation (calculated by root-mean-square method); ICC, intraclass correlation coefficient; IQR, interquartile range; SaO<sub>2</sub>, transcutaneous arterial oxygen saturation; SD, standard deviation. \* denotes variables with skewed distribution.

### Figure S2

Figure 2S shows Bland-Altman plots for comparisons between the three reliability STS tests (STS<sub>2a</sub> vs. STS<sub>2b</sub> and STS<sub>2b</sub> vs. STS<sub>2c</sub>).